Bandolier 46

What do we think?
What do we know?
What can we prove?

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Who blows your whistle?

Winston Churchill never read newspapers. His wife used to read the newspaper for him and then give him a précis plus important cuttings. Clementine, adding wisdom, probably made a better job of converting information to knowledge than the software. It was a system that prevented him being deluged by paper and having the "frog in a jam jar" feeling.

David Halberstam's brilliant book, 'The Brightest and The Best', has some marvellous insights into how institutions can stifle individuals. Individuals who did not agree with American Government policy on the Vietnam War were systematically sidelined. The information, the knowledge, which they produced to show that the policies were ineffective, was discarded in favour of the military bluff. The ability of individuals to speak out, even though we may think their views are crazy, is very precious.

Accepting change

It is by listening to whistleblowing that we can make progress through a process of constructive disagreement. Constructive disagreement is particularly important when we examine the evidence-base of what we do now or plan to do in the future. Change is often disagreeable, and it is surprising that in an area like healthcare where change is the rule rather than the exception, that we do not have more information on change management.

Where we do not believe

In ***Bandolier*** 42 we ran a Question Time to see if readers' questions for which we could not find answers were answerable by others. About half the questions attracted responses of various sorts, which were passed on to the questioners, but there was insufficient evidence for a ***Bandolier*** article. One was more interesting, the use of glucosamine in arthritis.

It seemed at first that there was little evidence, and that perhaps it was negative. But we eventually found quite a number of papers (most were in the latest issue of the Cochrane Library), and so this issue has a brief review of what ***Bandolier*** was able to find. The bottom line is that it seems to work.

So, just like Hypericum for depression (***Bandolier*** 31), an unconventional approach seems to be effective. But other conventional and unconventional approaches are not supported by evidence. For instance, we report another nail in the coffin of homeopathy this month. So headaches for believers and unbelievers alike, and difficult decisions for policy makers, patients, and their carers.

GLUCOSAMINE AND ARTHRITIS

In ***Bandolier***'s Question Time (***Bandolier*** 42), Dr Proctor from Gainsborough asked what evidence there was that glucosamine was an effective treatment for arthritis. Given the amount of publicity it had been getting, we thought this was a good question. We had a number of responses, and decided to follow this up by trying to find papers and assess what evidence we could find.

Searching

This involved MEDLINE searching for articles on glucosamine, finding Internet pages which featured glucosamine, reference lists from retrieved articles, and references provided by ***Bandolier*** readers.

Results

Eight randomised trials [1-8] involving oral or intramuscular glucosamine were found and the details are in the large Table on page 3. Articles on intra-articular injection, or where the material used was not clearly defined as glucosamine were excluded, as were non-randomised case series. All those included examined oral and/or intramuscular glucosamine in patients with arthritis over periods of up to eight weeks. Most had well-described methods and six had quality scores of 3 or more on a five-point scale [9]. Oral doses of glucosamine sulphate were 1.5 grams a day, and intramuscular doses were 400 mg twice or three times a week.

Placebo-controlled trials

Five trials compared glucosamine with placebo. All showed statistical superiority of glucosamine. Four of these had dichotomous outcomes for calculating NNTs, which ranged from 1.7 to 6.3 in individual trials. Overall the NNT was 5.0 (3.5 to 8.9). This means that one of every five patients with

In this issue

Outcomes for oral or intramuscular glucosamine in arthritis

Trial	Administration	Outcome	Glucosamine response	Placebo response	NNT (95% CI)
Pujalte et al, 1980	Oral	Improved pain and tenderness at 6-8 weeks	8/10	2/10	1.7 (1.1 to 4.0)
Crolle & D'Este, 1980	Oral	Symptom free at 3 weeks	4/15	0/15	3.8 (2.0 to 27)
Rovalti, 1992	Oral	Responder at 4 weeks	66/126	46/126	6.3 (3.6 to 26)
Reichelt et al, 1994	Intramuscular	Responder at 6 weeks	40/79	23/76	4.9 (2.8 to 19)
Combined			118/230	71/227	5.0 (3.5 to 8.9)

arthritis who are treated with glucosamine, one would have short term benefits in reduced pain and tenderness who would not have had if they had been given a placebo.

Active-controlled trials

Three trials compared glucosamine with NSAID (phenylbutazone or ibuprofen). There was no difference between ibuprofen (1.2 g/day) and oral glucosamine (1.5 g/day).

Adverse effects

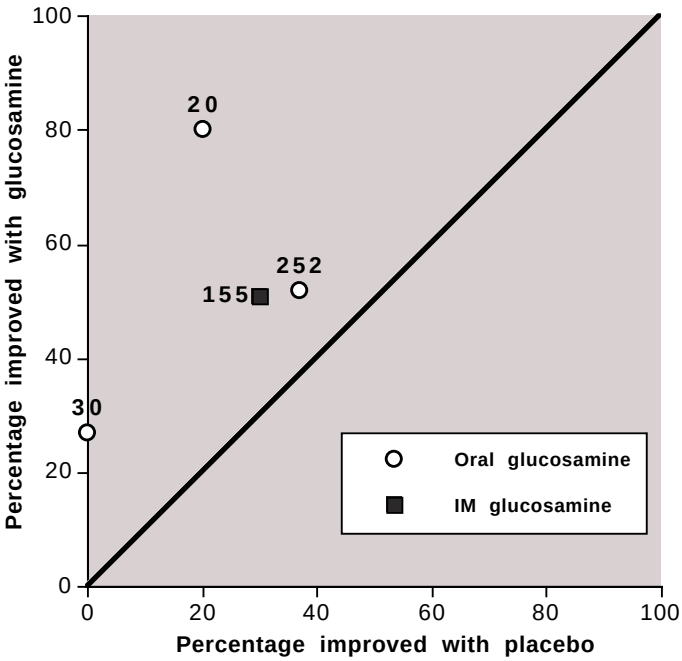
Few adverse effects or study withdrawals were reported for glucosamine. They tended to occur less frequently with glucosamine than with NSAID. A large open study of 1208 arthritis patients taking oral glucosamine 1.5 g/day for 13 to 99 days [10] had 28 patients who stopped taking glucosamine because of adverse effects. Those adverse effects reported in more than 1% of patients were epigastric pain/tenderness, heartburn, diarrhoea and nausea.

Comment

Bandolier was surprised to find as many as eight randomised trials. While it is possible to criticise all of the trials to some extent, as a group they are no worse than others used to support commonly-used therapies. There is a consistent thrust of efficacy over placebo, and an inability to distinguish glucosamine from NSAID. But all trials were relatively short-term, and longer-term observations for adverse effects would be welcome.

The bottom line is that there is a body of evidence supporting the efficacy of oral and intramuscular glucosamine in arthritis.

Trials of oral and intramuscular glucosamine vs placebo



References:

1 W-D Mund-Hoyn. Konservative behandlung von Wirbelsäulenarthrosen mit glucosaminsulphat un phenylbutazone. Therapiewoche 1980 30: 5922-8.

2 JM Pujalte, EP Llavore, FR Ylescupidez. Double-blind clinical evaluation of oral glucosamine sulphate in the basic treatment of osteoarthrosis. Current Medical Research and Opinion 1980 7: 110-4.

3 G Crolle, E D'Este. Glucosamine sulphate for the management of arthrosis: a controlled clinical investigation. Current Medical Research and Opinion 1980 7: 114-9.

4 E D'Ambrosio, B Casa, R Bompani, G Scali, M Scali. Glucosamine sulphate: a controlled clinical investigation in arthrosis. Pharmacotherapeutica 1981 2: 504-8.

5 AL Vaz. Double-blind clinical evaluation of the relative efficacy of ibuprofen and glucosamine sulphate in the management of osteoarthrosis of the knee in outpatients. Current Medical Research and Opinion 1982 8: 145-9.

6 LC Rovati. Clinical Research in osteoarthritis: design and results of short-term and long-term trials with disease-modifying drugs. International Journal of Tissue Reaction 1992 XIV: 243-51.

RANDOMISED CONTROLLED TRIALS OF ORAL AND INTRAMUSCULAR GLUCOSAMINE

Reference	Patients	Design	Drugs & Doses	Outcomes	Results	Quality score
Mund-Hoym, 1980	80 patients with "vertebralsyndome". Mean age 58 years	Randomised, parallel-group	3 injections of 400 mg glucosamine sulphate a week, plus oral glucosamine 250 mg 2/3 times a day on non-injection days (40 patients) Daily injections of 600 mg phenylbutazone (40 patients) All IM injections	Number of days to clinical improvement. Global good/bad	Glucosamine 32 days (± 1.3, range 21 - 48). Phenylbutazone 46 days (± 1.7, range 27 - 80). Good/bad outcome 34/6 for glucosamine, 29/11 for phenylbutazone	
Pujalte et al, 1980	24 patients with osteoarthritis of the knee. Mean age 60 years	Randomised, double-blind, parallel-group, 6-8 weeks	500 mg glucosamine sulphate, three times daily or identical placebo No other analgesics allowed	Articular pain, swelling, movement using categorical scale (patient and doctor)	Glucosamine significantly ($p<0.01$) better than placebo for pain, tenderness and swelling. Time for clinical improvement 14 days for glucosamine cf 40 days for placebo. No AE with glucosamine.	
Crolle & D'Este, 1980	30 in-patients with chronic osteoarthrosis. Mean age 72 years	Randomised, double-blind, parallel-group, 21 days	400 mg intramuscular glucosamine sulphate for 7 days, followed by 500 mg orally three times a day for 14 days. IM piperazine/chlorbutanol for 14 days, followed by oral placebo for 14 days.	Pain at rest or movement, categorical scale. Walking time over 20 metres.	Glucosamine significantly ($p<0.01$) better than placebo for pain and function restriction at 21 days. Overall symptom score better with glucosamine. No difference in walking times, though better. No AE.	
D'Ambrosio et al, 1981	30 in-patients with chronic degenerative osteoarthrosis. Mean age 75 years. No steroids or NSAIDs for 2 weeks before trial.	Randomised, open, parallel-group, 21 days	400 mg intramuscular glucosamine sulphate for 7 days, followed by 500 mg orally three times a day for 14 days. IM piperazine/chlorbutanol for 14 days, followed by oral placebo for 14 days.	Pain at rest or movement, categorical scale.	Glucosamine significantly ($p<0.01$) better than placebo for symptom score at 21 days. (pain at rest and movement appear significantly improved, though no stat test done). No AE.	
Vaz, 1982	40 out-patients with unilateral osteoarthritis of the knee without complications. Mean age 58 years.	Randomised, double-blind, parallel-group, 8 weeks	1.5 g/day of glucosamine sulphate or 1.2 g ibuprofen.	Pain. categorical scale.	Ibuprofen significantly better than glucosamine at 2 weeks, glucosamine significantly better than ibuprofen at 8 weeks. AE (mild) reported by 2 on glucosamine and 5 on ibuprofen. Overall efficacy (doctor) good 8/18 glucosamine and 3/20 ibuprofen.	
Rovalti, 1992, Study 1	252 out-patients with gonarthrosis.	Randomised, double-blind, parallel-group, 4 weeks	1.5 g/day of glucosamine sulphate or placebo.	Lesquesne index, responders/non-responders	Glucosamine significantly ($p<0.05$) better than placebo for symptom score at 4 weeks. Responders 66/126 glucosamine, 46/126 placebo. Minor AE 8/126 glucosamine, 13/126 placebo.	
Reichelt et al, 1994 (duplicated in Rovalti, 1992, Study 2)	155 out-patients with gonarthrosis.	Randomised, double-blind, parallel-group, 6 weeks	Intramuscular glucosamine sulphate 400 mg or placebo twice a week.	Lesquesne index, responders/non-responders	Glucosamine significantly ($p<0.04$) better than placebo for symptom score at 4 weeks. Responders 40/79 glucosamine, 23/76 placebo. Minor AE 5/79 glucosamine, 3/76 placebo.	

7 H Müller-Fassbender, GL Bach, W Haase, LC Rovati, I Setnikar. Glucosamine sulphate compared to ibuprofen in osteoarthritis of the knee. Osteoarthritis and Cartilage 1994 2: 61-9.

8 A Reichelt, KK Fuorster, M Fischer, LC Rovati, I Setnikar. Efficacy and safety of intramuscular glucosamine sulphate in osteoarthritis of the knee. Arzneim-Forsch/Drug Research 1994 44: 75-80.

9 AR Jadad, RA Moore, D Carroll, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Controlled Clinical Trials 1996 17: 1-12.

10 MJ Tapadinhas, IC Rivera, AA Bignamini. Oral glucosamine sulphate in the management of arthrosis: report on a multi-centre open investigation in Portugal. Pharmacotherapeutica 1982 3: 157-68.

CONSTIPATION

We all know what it is, but it is hard to define. Bowel movement patters show that 90% of people in Western countries have between three bowel movements a day to three per week. Constipation is often defined as fewer than three bowel movements a week, though symptoms like straining, passing hard stools and inability to defecate when desired, together with abdominal pain also form part of a diagnosis.

The use of laxatives, both prescribed and non-prescribed, is common, and constipation is thought to be common, especially in older people, women, and people with poor diets. So one might think that there would be a wealth of information from clinical trials on the effectiveness of laxative agents - that we would know that they work, and how well they work.

Bandolier thought so too. So it was a surprise to see from a systematic review [1] that we don't have as much information as we thought, or would like.

Review

This is a good review, with great searching (though some might quibble about the exclusion of reports not in English), and an interesting description about a large number of trials which did not pass muster for various reasons. It makes a good read, though the journal is not readily available and ***Bandolier*** had to obtain it through the British Library.

Trials were included if they looked at treatment of constipation in adults for at least two weeks (minimum of one week on treatment or control).

Results

They found 36 trials with 1,815 subjects, of whom 40% were over 60 years, and 70% of whom were women. Many of the trials had poor design. There were 25 different laxative or dietary fibre therapies. Twenty trials compared laxative with placebo or regular diet, and 16 were comparisons with other laxatives.

Bowel movements

The number of bowel movements per week in controls ranged from a mean (or median) of 1.5 to 7.1. Only six of 16 reports had mean bowel movements per week below 3. Laxatives increased the number of bowel movements (Figure) from a control mean (weighted by number of patients) of 3.5 per week to 5.0 per week. The increase was 1.4 bowel movements per week (95% confidence interval 1.1 to 1.8).

Bulk laxatives (six trials) gave an average weighted mean increase of 1.4 (0.6 to 2.2), and other agents (seven trials) gave a weighted mean increase of 1.5 (1.1 to 1.8).

Overall symptom improvement was reported as being significantly better for laxatives than control in nine of eleven trials which measured them.

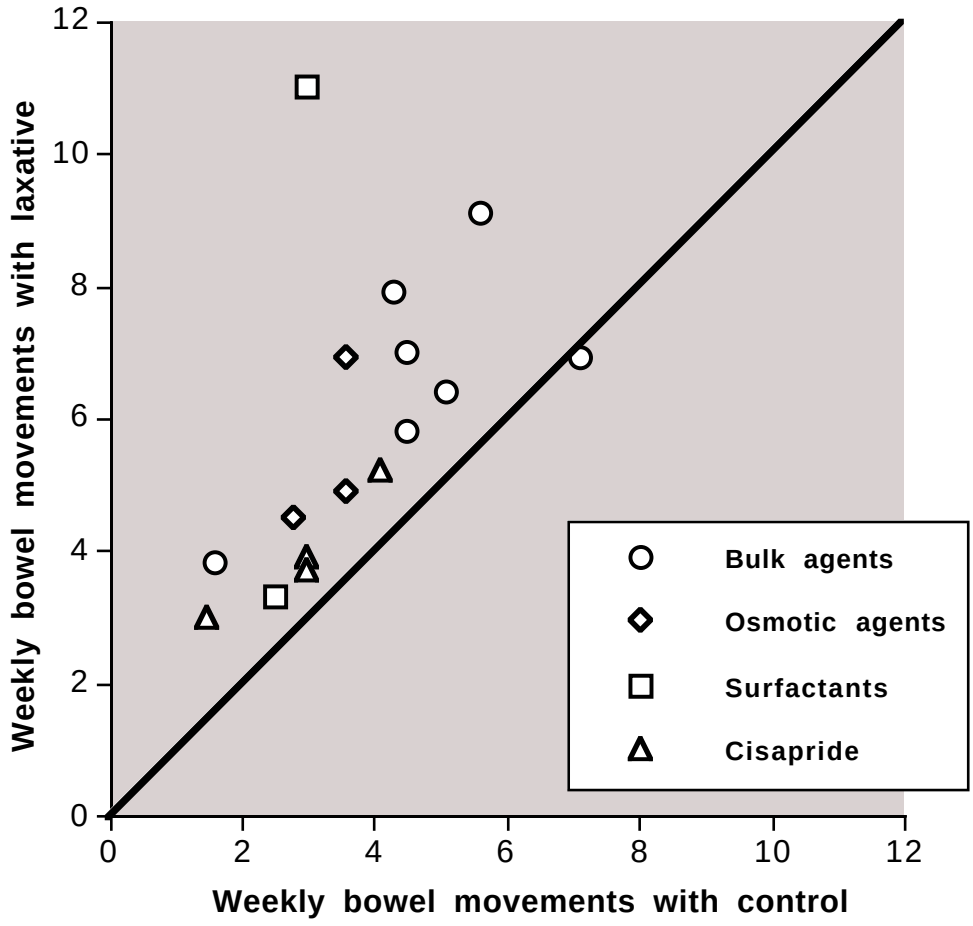
Results from the trials which compared different laxatives were largely uninterpretable.

Comment

Laxatives work. Perhaps there's nothing new in that. What is disappointing is that there is so little evidence to allow us to see which is best. What we can say is that for adult patients with chronic constipation, bran or bulk laxatives work as well as anything. The amount of bran used in the trials ranged from 0.5 gram to 24 grams a day, equivalent to from a quarter of a serving of fruit, vegetables or cereal a day to 12 servings a day. Advising adults with chronic constipation to eat more fruit and vegetables and have some bran seems to be the best evidence available.

References:
1 SM Tramonte, NB Brand, CD Mulrow et al. The treatment of chronic constipation: a systematic review. Journal of General Internal Medicine 1997 12: 15-24.

Effect of laxatives on the number of weekly bowel movements



More on BPH

Treatment of benign prostatic hypertrophy has been further informed by a meta-analysis and a large randomised controlled trial (RCT). The meta-analysis looked at results after one year on finasteride or placebo, and the RCT examined effects after two years of treatment. ***Bandolier*** has a quibble with both of these reports. Each has lovely statistics and large numbers, but both lack a clear statement of what constitutes clinical improvement in men with BPH, either in terms of peak urine flow rate, or in terms of symptom scores. And without that, and with just means, no NNTs can be calculated from the published data, which is disappointing considering the quality of the studies.

Meta-analysis

This examined one-year results of six RCTs comparing finasteride and placebo [1]. There were 2601 men randomised between finasteride 5 mg or placebo daily for one year. Prostate volume was measured by trans-rectal ultrasound (TRUS) or MRI.

The bottom line was that finasteride is only effective in men with prostate volumes of more than 40 mL. The Figure shows data from a single patient analysis for peak urine flow rate, though a similar picture emerges for symptom scoring. The conclusion was that men with small prostates may not be suitable candidates for finasteride therapy.

RCT - two year outcomes

The RCT enrolled 707 men with moderate symptoms of BPH and treated them with 5 mg finasteride or placebo daily for two years.

The main results were that men on placebo had worsening symptom scores and urine flow rates in the second year of treatment, whereas men on finasteride maintained the benefits seen in the first year of treatment. There was sufficient information to calculate some NNT values (Table). For instance, prostate volumes increased in 56% of men on placebo, but only 16% of men on finasteride. The NNT of 2.5 indicates that finasteride has to be given to five men for two years to prevent an increase in prostate volume of more than 1 mL in two, in whom this would not have been prevented with placebo.

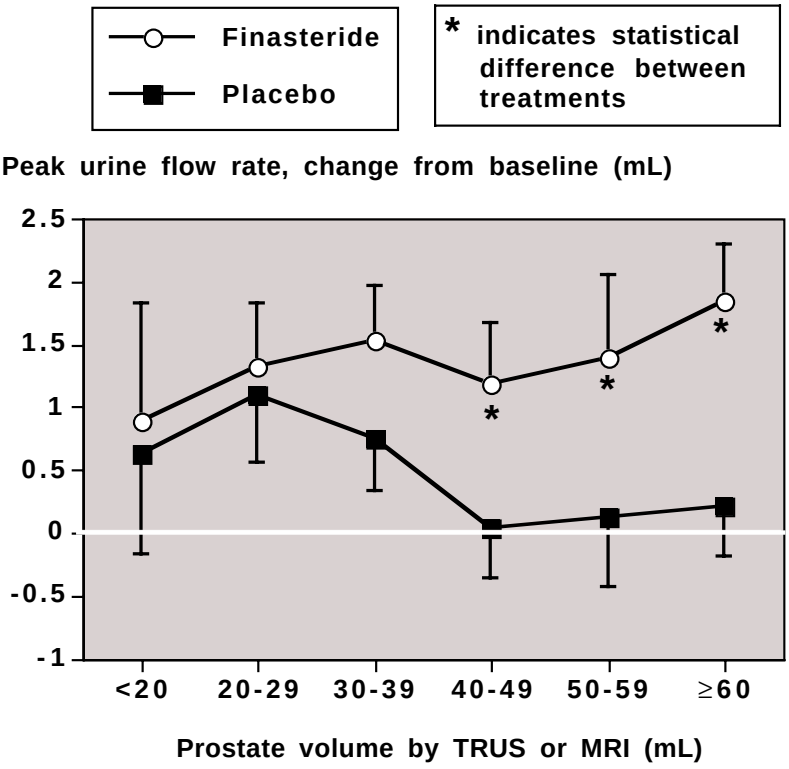
One patient in 30 to 40 would stop the drug because of insufficient response, or because of urinary retention or surgery. For finasteride to cause one case of sexual dysfunction had an NNT of 11.

Comment

The accumulating information on finasteride treatment of BPH is giving more clear indications on which men can benefit (those with prostate volumes >40 mL) and that the benefits seen in one-year studies continue at least to two years. The lack of information to calculate NNTs for clinically relevant outcomes (and what they might be) still eludes us.

References:
1 P Boyle, AL Gould, CG Roeherborn. Prostate volume predicts outcome of treatment of benign prostatic hyperplasia with finasteride: meta-analysis of randomized clinical trials. Urology 1996 48: 398-405.
2 JT Andersen, P Ekman, H Wolf et al. Can finasteride reverse the progress of benign prostatic hyperplasia? A two-year placebo-controlled study. Urology 1995 46: 631-7.

Meta-analysis of six RCTs, effect of finasteride and placebo on peak urine flow rate at one year



Finasteride versus placebo for BPH: two-year outcomes

Outcome	NNT (95%CI)
Prevent prostate volume increase >1 mL	2.5 (2.1 to 3.2)
Prevent one patient developing urinary retention	32 (18 to 136)
Prevent one patient having prostate surgery	39 (23 to 111)
Prevent one patient discontinuing because of insufficient response	39 (17 to no difference)
Cause one case of sexual dysfunction	11 (6.9 to 23)

SIGNS AND SYMPTOMS PREDICT THYROID DISEASE

On the face of it this headline has all the impact of "dog bites man". But one of the problems that clinical laboratories face, as they have for years, is the overwhelming tide of tests. When all they could offer was basic metabolic rate (and those old enough will remember how difficult they were to do), patients had full clinical workups before the test was done. A simple blood test is just that, simple, so anyone with any possibility of disease is investigated. All laboratories have a library of what they would regard as stupid reasons for requesting thyroid function tests - ingrowing toenail is one ***Bandolier*** remembers.

So some simple words from 20 years ago about the relationship between clinical signs and symptoms and the incidence of thyroid disease [1] are still relevant.

Study

Five-hundred consecutive inpatients and outpatients (those with known thyroid disease being excluded) to Flinders Medical Centre had case notes examined for:

- thyroid function test (TFT) results.
- clinical signs and symptoms noted by the clinician during the consultation from which the referral for TFT was made.
- subsequent clinical diagnosis of thyroid status.

The degree of clinical suspicion from signs and symptoms from a generally accepted (see box) list was correlated with final outcome.

Results

Of the 500 patients, 21 (4.2%) were found to have thyroid dysfunction needing treatment.

In those patients with five or more clinical signs or symptoms in whom the degree of clinical suspicion was high, the majority (18, 78%) had thyroid disorder needing treatment. Using final diagnosis as the gold standard, the likelihood ratio for having a high degree of clinical suspicion was 82. This meant that from a pre-test probability of 4.2% the post-test probability was over 80%.

In those with high or intermediate degree of clinical suspicion, 19 (33%) had thyroid disorder needing treatment. Using final diagnosis as the gold standard, the likelihood ratio for having a high or intermediate degree of clinical suspicion was 11. This meant that from a pre-test probability of 4.2% the post-test probability approached 40%.

In those with low degree of clinical suspicion, 2 of 442 patients (0.45%) had thyroid disorder needing treatment. Using final diagnosis as the gold standard, the likelihood ratio for having a low degree of clinical suspicion was 0.1 (calculated as the likelihood ratio of a negative test). This meant that from a pre-test probability of 4.2% the post-test probability was less than 1%.

Signs, symptoms and clinical suspicion of thyroid dysfunction

1 **Thyroid**

Goitre, thyroid bruit, fine tremor, weight loss, increased appetite, lid lag, sweating, heat intolerance, family history, lethargy, weight gain, hoarseness, dry skin, hair loss, cold intolerance, delayed reflex, constipation, short stature.

2 **Cardiovascular**

Recent myocardial infarction, chronic cardiac failure, coronary artery disease, arrhythmias, pulse >90/min, hypertension.

3 **Others**

Pneumonia, asthma, diabetes.

Degree of clinical suspicion

High

Patient presenting with 5 or more signs/symptoms listed in groups 1 and 2.

Intermediate

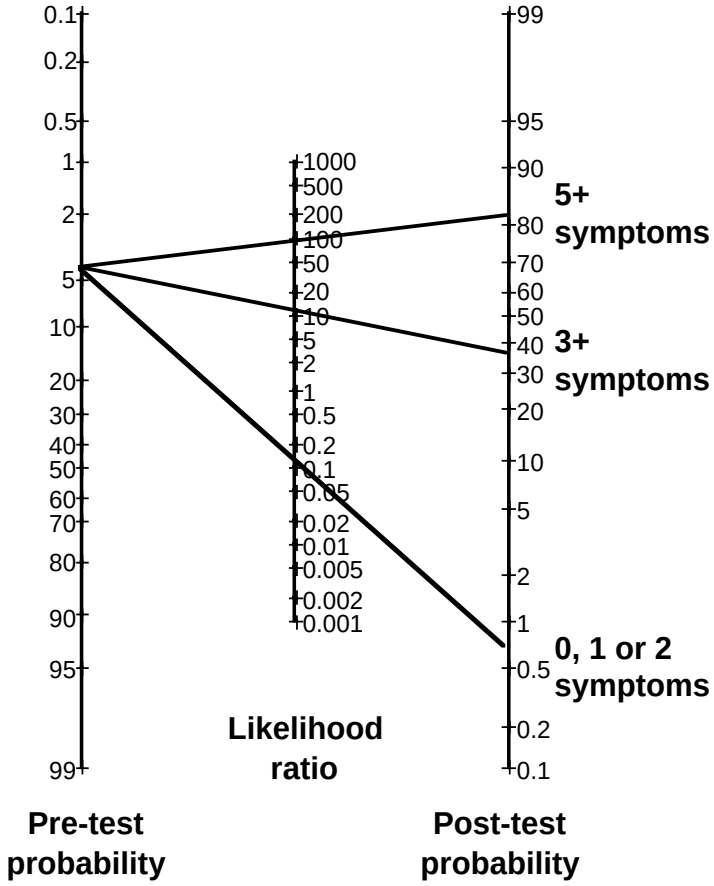
Patient presenting with 3 or 4 signs/symptoms listed in groups 1 and 2.

Low

Patient presenting with 1 or 2 signs/symptoms listed in groups 1, 2 and 3.

Degree of suspicion	Number of patients	Number with thyroid disease	Percent with thyroid disease
High	23	18	78
Intermediate	35	1	2.9
Low	442	2	0.45
Total	500	21	4.2

Likelihood ratio nomogram signs & symptoms of thyroid disease



Comment

"Look at the relative size of the likelihood ratios for a brief, immediate, relatively cheap history and a much longer, delayed, and relatively expensive exercise electrocardiogram. There is no contest. Likelihood ratios for key points in the history and physical examination, both for this and for most other target disorders, are mammoth and dwarf those derived from most excursions through high technology."[2]

Bandolier has always found these words comparing clinical examination and exercise testing compelling, but has struggled to find examples. Thyroid function testing appears to be one. Of course, these are "old" data, but Australian patients being examined in 1977 won't be that different from people in the UK in 1997.

Since the incidence of thyroid disease in the general population is the order of 1% or below, some selection has already gone on to create a 4.2% incidence in the population in the paper. But that serves only to emphasise the very low yield of thyroid disease (0.45%) in those patients in whom there was a low clinical suspicion. It prompts the question, why do a TFT? But post-test probabilities of more than 30% for at least 3 signs and symptoms, and of more than 80% for at least 5 signs and symptoms would seem to make TFTs worthwhile in confirming the diagnosis.

The authors discuss the "heavy economic and logistic burden of biochemical screening" that biochemical screening was causing. Plus ça change.

References:
1 GH White, RN Walmsley. can the initial clinical assessment of thyroid function be improved? Lancet 1978 ii: 933-5.
2 Clinical Epidemiology (Eds DL Sackett, RB Haynes, GH Guyatt, P Tugwell), 2nd Edition, 1991, p132.

OLD CURIOSITY SHOP

The power of prayer

Many people of different faiths believe that prayer can have beneficial effects on their own or others' health. Testing the power of prayer is not easy, but a randomised, double-blind trial with large numbers demands some attention.

Study

During a 10-month period in 1982/3, patients admitted to San Francisco General Hospital coronary care unit were eligible for entry. Of these, 393 entered the trial and 57 did not want to participate after being fully informed about the nature of the project.

Intercessionory prayer was provided by "born again" Christians of several denominations. After randomisation (by computer-generated list), patients in the prayer group were prayed for by between three and seven intercessors. The intercessors were given the first name, diagnosis and general condition of the patient, with pertinent updates. Prayer took place outside the hospital daily until discharge. Intercessors prayed for a rapid recovery, and for prevention of complications and death, as well as anything else they wanted to add to the prayer.

Patients had no idea whether or not they were being prayed for. Additional prayers in either group by, for instance, family members, was not controlled for. Data on patients' condition, complications and outcome was collected blind.

Results

There were no differences at entry between patients for any demographic variable, primary cardiac diagnosis, or noncardiac illness or complication.

Intercessionory prayer was without effect on days spent in the coronary care unit, or days in hospital, or number of discharge medications. There were 26 new problems, diagnoses or therapeutic events monitored after entry into the trial; 107 events occurred in 192 patients being prayed for and 175 occurred in 210 control patients. Six events occurred significantly less frequently with prayer - congestive heart failure, use of diuretics, cardiac arrest, pneumonia, antibiotic use and intubation or ventilation.

The clinical course of patients was scored as good, intermediate, or bad according to a scoring system. Good outcomes were more frequent in patients who were being prayed for (163/192; 85%) than in those who were not prayed for (147/201; 73%). This generated a relative benefit of 1.16 (1.05 - 1.29) and a NNT of 8.5 (5.1 - 26).

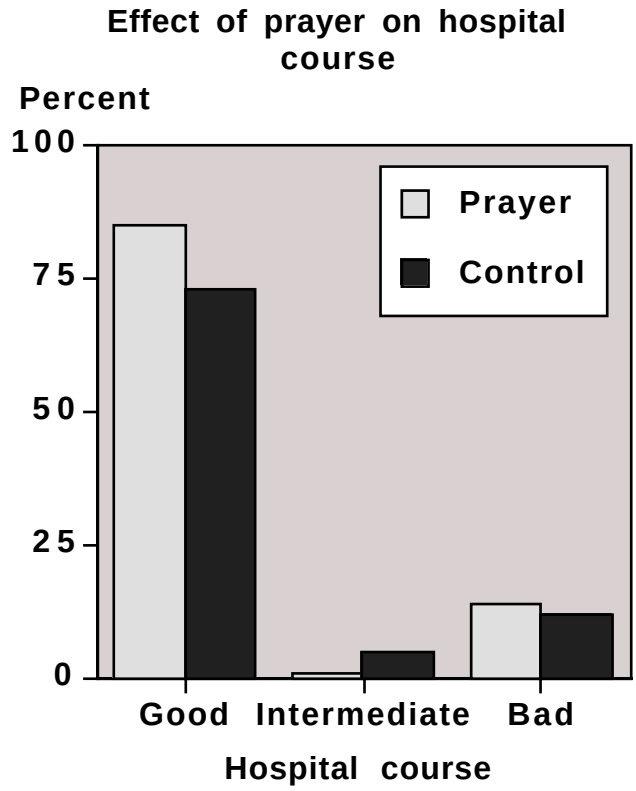
Comment

People will be able to see what they want from this trial. It was a properly randomised, double-blind trial. It had statistically significant outcomes in favour of prayer having a beneficial effect in this patient group. There were no outcomes for which the control group did better than those being prayed for, and though the effects are not great, they all go in one direction, that prayer is effective.

Doubters might point out that there may have been an element of data-dredging, because there was no prior statement of what outcomes were going to be looked at, and so we have to look less favourably on the result. They may also point out that some of the events where statistical significance was found were fairly rare, occurring in only a few percent of patients in both groups, so random chance may play a part.

The lesson is that a single trial is just that, one observation. If the effect was massive, and the trial huge, and there was an agreed and understood mechanism, then perhaps taking results from a single trial may be OK. Where these conditions are not met, then caution rules. The fact that a Cochrane review group is summarising all the literature on the effects of prayer is welcome.

Reference:
1 Positive therapeutic effects of intercessionory prayer in a coronary care unit population. Southern Medical Journal 1988 81: 826-9.



Another headache for homeopathy

Bandolier 45 featured the results of a large meta-analysis on homeopathy - with results at best described as mediocre, and pointing out that high quality trials did poorly. A new trial, of exquisite design comes up with a barn door negative for homeopathy.

Design

The study will make a delightful read for trial design aficionados. Briefly after agreement on homeopathic treatment by six practitioners, patients with regular long-standing headaches had homeopathic remedy or placebo dispensed from a notary public who held the randomisation schedule and mailed out the treatments. Reporting was to a study secretariat unconnected with the patients. All steps to maintain randomness and blindness that could be taken were taken.

Results

Though headache frequency declined in all patients, there was no difference between homeopathy and placebo on any measure. Chalk another one to solid trial design.

Reference:
1 H Walach, W Haeusler, T Lowes et al. Classical homeopathic treatment of chronic headaches. Cephalalgia 1997 17: 119-26.

Diary note

The ***Bandolier*** conference on Chlamydia had had to be postponed. It will now take place on March 27, 1998, at the Wellcome Institute in London.

Details can be obtained from Eileen Neail, preferably by fax on 01865 226978.

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